REMARKS:

In the Office Action dated September 15, 2009, claims 1, 3-8, 11-16, 20, 32-36 and 38-44, in the above-identified U.S. patent application were rejected. Reconsideration of the rejections is respectfully requested in view of the above new claims and the following remarks. Claims 1-44 have been canceled without prejudice or disclaimer and new claims 45-92 have been added to the application. Support for new claims 45-92 can be found throughout the application, at least at page 4, lines 25-30, page 5, lines 15-30, and page 30, lines 12-22, in the present application. Thus, the new claims are supported by the specification as filed and do not add new matter. Applicants respectfully submit that the outstanding rejections of claims 1, 3-8, 11-16, 20, 32-36 and 38-44 should not be applied to new claims 45-92.

Rejections under 35 USC §102(e)

Claims 1, 3-8, 11-16, 20, 32-36 and 38-42 were rejected under 35 USC §102(e) as allegedly anticipated by McSwiggen et al. (McSwiggen). Solely to advance prosecution, claims 1, 3-8, 11-16, 20, 32-36 and 38-44, have been cancelled and thus, this rejection is moot. Applicants respectfully submit that new claims 45-92 are not anticipated by McSwiggen.

The Examiner asserts that "McSwiggen explicitly taught that RNAi-mediating RNA molecules can be prepared as a single-stranded RNA comprising a nucleotide sequence that is capable of forming a self-complementary hairpin double-stranded RNA." Office Action mailed September 15, 2009 (Office Action) at page 3 (citing McSwiggen at paragraph 0027). The present claims to "single-stranded" compounds do not read on such

self-complementary hairpin double-stranded" molecules and thus, are not anticipated by McSwiggen.

During prosecution, claims are given their "broadest reasonable interpretation consistent with the specification." MPEP § 904. However, interpretation of the term "single-stranded" to include self-complementary strands that form a double-stranded duplex is not consistent with the present specification.

Paragraphs 003-009 discuss mechanisms in which siRNA duplexes were known to activate the RISC pathway, and contrasts such "duplexes" from "single-stranded" molecules. For example, the specification remarks that the siRNA duplex must be unwound prior to target recognition, however, it was unknown whether the "unwound strands of an siRNA duplex remain associated with RISC or whether RISC only contains a single-stranded siRNA." Specification at paragraph 007. The specification further remarks that, "[i]ntroducing 5' phosphorylated single-stranded antisense siRNAs into HeLa cells potently silences endogenous gene with similar efficiency than duplex siRNA." Id at paragraph 9. Such use of the term "single-stranded" precludes a meaning that encompasses duplexes.

Moreover, the specification directly discusses self-complementary hairpin structures, and again contrasts such molecules with "single-stranded" molecules as claimed. For example, the specification at page 16, lines 21 to page 17, line 4, (paragraph 0060) indicates that that "[A]lternatively to the application of siRNAs as synthetic double-stranded or single-stranded siRNAs, it is conceivable to also administer an antisense siRNA precursor molecule in the form of a hairpin stem-loop structure comprising 19 to 29 base pairs in the stem with or without 5' or 3' overhanging ends on one side of the duplex and a

nucleotide or non-nucleotide loop on the other end." This disclosure clearly indicates that a molecule with a hairpin stem and loop structure is not considered to be the same as a double-stranded or single-stranded siRNA in the present invention. In other words, the molecule with a hairpin stem and loop structure is a precursor of a siRNA molecule. This interpretation is also supported by original claim 30 which is an independent claim directed to an antisense siRNA **precursor** molecule which has a hairpin stem-loop structure.

In view of such disclosures in the specification, one skilled in the art would not reasonably interpret the term "single-stranded" as used in the present claims to include stem loop structures such as those discussed in McSwiggen. For at least that reason, McSwiggen does not anticipate the present claims. Accordingly, Applicants respectfully request that the rejection of claims 1, 3-8, 11-16, 20, 32-36 and 38-44 not be applied to any of new claims 45-92.

Claims 1, 3-8, 11-16, 20, 33-36 and 38-42 were rejected under 35 USC §102(e) as allegedly anticipated by US 2002/0150945 to Finney et al. (Finney). Claims 1-44 have been cancelled and thus, the rejection is moot. Applicants respectfully submit that new claims 45-92 are not anticipated by Finney.

Like McSwiggen, discussed above, Finney discusses self-complementary RNAi molecules that form double-stranded duplexes. See Finney at paragraph [0110]. As discussed above regarding McSwiggen, one skilled in the art would interpret the term "single-stranded" in the present claims, to exclude such double-stranded structures. For at least the reasons discussed above regarding McSwiggen, applicants contend that the present claims are not anticipated by Finney and request that this rejection not be applied to new claims 45-92.

Rejections under 35 USC §112

Claims 1, 3-8, 11-16, 20, 32-36, 38-42 and 44 were rejected under 35 USC §112, first paragraph, as allegedly lacking an adequate written description regarding the language "completely single stranded". Solely to advance prosecution and without acquiescing to the rejection, claims 1, 3-8, 11-16, 20, 32-36, 38-42 and 44 have been canceled. Thus, the rejection is moot. New claims 45-92 do not recite the language "completely single stranded." Accordingly, Applicants request that this rejection not be applied to new claims 45-92.

Claims 43-44 were rejected under 35 USC §112, first paragraph, as allegedly lacking enablement for a method using a single stranded siRNA molecule which is from 14-18 nucleotides in length. Applicants respectfully traverse.

To satisfy the enablement requirement, the specification must "teach those in the art to make and use the invention without 'undue experimentation'." In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988). However, the Federal Circuit has noted that the fact that "some experimentation may be required is not fatal; the issue is whether the amount of experimentation is 'undue'." In re Vaeck, 947 F.2d 488, 495 (Fed. Cir. 1991). The Examiner has not established that one of skill in the art could not practice the invention as claimed without undue experimentation.

The Examiner first remarks that the "instant application explicitly demonstrates that single-stranded siRNA of 15 nucleotides or 17 nucleotides in length . . . do not inhibit target expression in mammalian cells compared to a control siRNA." Office Action at page 7 (citing Figure 11 of specification). That is not correct. Actually, the 17 nucleotides-long single-stranded siRNA having a 5'-phosphate did reduce target expression compared to

control, though not as much as the longer molecules tested. Thus, although it is not required for enablement, the specification clearly demonstrates activity from a 17 nucleotide-long single-stranded siRNA. Further, although the 13 and 15 nucleotide-long molecules did not reduce target expression in the experiment shown in Figure 11, the success of longer molecules suggests that with optimization, shorter siRNA's within the claimed range could be identified without undue experimentation.

The Examiner attempts to rely on the Rule 1.132 Declaration of inventor T. Tuschl to bolster the assertion of non-enablement. See Office Action at page 7. The Examiner quotes Dr. Tuschl's remark that "it would have been hopeless to use short single-stranded RNA molecules for RNAi in mammalian systems." Id. The Examiner reasons that "[g]iven the incomplete knowledge pertaining to the technology based on the RNAi activity in a mammalian system mediated by a single-stranded, short siRNA . . . as acknowledged by applicant, and given the negative teachings pertaining to shorter than 19 nucleotides in length . . . undue amount of experimentation would have been necessitated for one of ordinary skill in the art at the time the invention was made." Id. The Examiner's attempted reliance on the inventor's declaration as evidence for non-enablement is misplaced. The declaration addresses obviousness, which is assessed at the time of invention, while enablement is assessed at the time of filing, with full view of the specification. Indeed, the Examiner truncated the Inventor's complete remark that "based on the literature available at the priority date of the present application, the skilled person would have concluded that it would have been hopeless to use short single-stranded RNA molecules for RNAi in mammalian systems." Declaration at paragraph 5 (emphasis added). The positive results reported in the specification for molecules 17-29 nucleotides in length change that

landscape. Once these data are considered, one of skill would no longer consider it "hopeless" to use single-stranded RNA molecules, including molecules as short as 14 nucleotides in length in mammalian cells. Rather, one would conclude that with routine experimentation, active single-stranded RNAi molecules from 14 to 50 nucleotides in length could be identified. Accordingly, Applicants respectfully request that the rejections of claims 43-44 under 35 USC §112, first paragraph not be applied to any of new claims 45-92.

Conclusion

Applicants respectfully submit that all of claims 45-92 are now in condition for allowance. If it is believed that the application is not in condition for allowance, it is respectfully requested that the undersigned attorney be contacted at the telephone number below.

In the event this paper is not considered to be timely filed, the Applicant respectfully petitions for an appropriate extension of time. Any fee for such an extension together with any additional fees that may be due with respect to this paper, may be charged to Counsel's Deposit Account No. 02-2135.

Respectfully submitted,

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